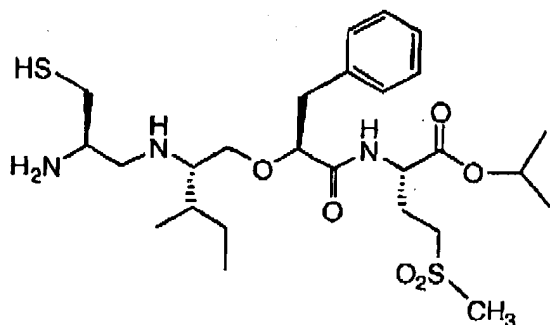


Applicants : W. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 18



75. (New) A pharmaceutical composition comprising an amount of a prenyl-protein transferase inhibitor and an amount of an antineoplastic agent selected from paclitaxel, epothilone A, epothilone B, desoxyepothilone A or desoxyepothilone B which is a microtubule-stabilizing agent, the composition which achieves a synergistic effect for treating cancer in a mammal in need thereof.

76. (New) A method of preparing a pharmaceutical composition which comprises mixing an amount of a prenyl-protein transferase inhibitor and an amount of an antineoplastic agent which is a microtubule-stabilizing agent selected from paclitaxel, epothilone A, epothilone B, desoxyepothilone A or desoxyepothilone B, said composition capable of achieving a synergistic effect for treating cancer in a mammal.

77. (New) A method for achieving a synergistic therapeutic effect in a mammal in need thereof which comprises administering to said mammal amounts of at least two therapeutic agents selected from a group consisting of:

- a) a prenyl-protein transferase inhibitor and
- b) an antineoplastic agent which is a microtubule-stabilizing agent selected from paclitaxel, docetaxel or epothilone; the synergistic therapeutic effect is the treatment of cancers of the brain, breast, colon, genitourinary tract, lymphatic system, pancreas, rectum, stomach, larynx, liver, lung, prostate, stat histiocytic lymphoma lung adenocarcinoma, pancreatic carcinoma, colorectal carcinoma, small cell lung cancers or neurological

Applicants : M. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 19

tumor cancer whose growth is inhibited by the administration of the prenyl-protein transferase inhibitor and the antineoplastic agent.

78. (New) The method according to Claim 77 wherein the prenyl-protein transferase inhibitor is selected from:

2(S)-Butyl-1-(2,3-diaminoprop-1-yl)-1-(1-naphthoyl)piperazine;

1-(3-Amino-2-(2-naphthylmethylamino)prop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-{5-[1-(2-naphthylmethyl)]-4,5-dihydroimidazol)methyl-4-(1-naphthoyl)piperazine;

1-[5-(1-Benzylimidazol)methyl]-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(5-[1-(4-nitrobenzyl)]imidazolylmethyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(3-Acetamidomethylthio-2(R)-aminoprop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[2-(1-imidazolyl)ethyl]sulfonyl-4-(1-naphthoyl)piperazine;

2(R)-Butyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-4-(1-naphthoyl)-1-(3-pyridylmethyl)piperazine;

1-2(S)-butyl-(2(R)-(4-nitrobenzyl)amino-3-hydroxypropyl)-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-hydroxyheptadecyl)-2(S)-butyl-4-(1-naphthoyl)-piperazine;

2(S)-Benzyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-(3-benzylthio)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

Applicants : R. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 20

1-(2(R)-Amino-3-[3-(4-nitrobenzylthio)propyl])-2(S)-butyl-4-(1-naphthoyl)piperazine;
2(S)-Butyl-1-[(4-imidazolyl)ethyl]-4-(1-naphthoyl)piperazine;
2(S)-Butyl-1-[(4-imidazolyl)methyl]-4-(1-naphthoyl)piperazine;
2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl]acetyl]-4-(1-naphthoyl)piperazine;
2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl]ethyl]-4-(1-naphthoyl)piperazine;
1-(2(R)-Amino-3-hydroxypropyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
1-(2(R)-Amino-4-hydroxybutyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
1-(2-Amino-3-(2-benzyloxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
1-(2-Amino-3-(2-hydroxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
1-[3-(4-imidazolyl)propyl]-2(S)-butyl-4-(1-naphthoyl)-piperazine;
2(S)-n-Butyl-4-(2,3-dimethylphenyl)-1-(4-imidazolylmethyl)-piperazin-5-one;
2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimethylphenyl)piperazin-5-one;
1-[1-(4-Cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimethylphenyl)-2(S)-(2-methoxyethyl)piperazin-5-one;
2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(1-naphthylmethyl)imidazol-5-ylmethyl]-piperazine;
2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(2-naphthylmethyl)imidazol-5-ylmethyl]-piperazine;

Applicants : N. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 21

2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

2(S)-n-Butyl-1-[1-(4-methoxybenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

2(S)-n-Butyl-1-[1-(3-methyl-2-butenyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

2(S)-n-Butyl-1-[1-(4-fluorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

2(S)-n-Butyl-1-[1-(4-chlorobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

1-[1-(4-Bromobenzyl)imidazol-5-ylmethyl]-2(S)-n-butyl-4-(1-naphthoyl)piperazine;

2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethylbenzyl)imidazol-5-ylmethyl]-piperazine;

2(S)-n-Butyl-1-[1-(4-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine;

2(S)-n-Butyl-1-[1-(3-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine;

1-[1-(4-Phenylbenzyl)imidazol-5-ylmethyl]-2(S)-n-butyl-4-(1-naphthoyl)-piperazine;

2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(2-phenylethyl)imidazol-5-ylmethyl]-piperazine;

2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethoxy)imidazol-5-ylmethyl]piperazine;

1-([1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl)-2(S)-n-butyl-4-(1-naphthoyl)piperazine;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(methanesulfonyl)ethyl]-2-piperazinone;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)ethyl]-2-piperazinone;

Applicants : W. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 22

(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

(S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[N-ethyl-2-acetamido]-2-piperazinone;

(±)-5-(2-Butynyl)-1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

5(S)-Butyl-4-[1-(4-cyanobenzyl-2-methyl)-5-imidazolylmethyl]-1-(2,3-dimethylphenyl)-piperazin-2-one;

4-[1-(2-(4-Cyanophenyl)-2-propyl)-5-imidazolylmethyl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonylethyl)piperazin-2-one;

5(S)-n-Butyl-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-1-(2-methylphenyl)piperazin-2-one;

4-[1-(4-Cyanobenzyl)-5-imidazolylmethyl]-5(S)-(2-fluoroethyl)-1-(3-chlorophenyl)piperazin-2-one;

4-[3-(4-Cyanobenzyl)pyridin-4-yl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonylethyl)-piperazin-2-one;

4-[5-(4-Cyanobenzyl)-1-imidazolylethyl]-1-(3-chlorophenyl)piperazin-2-one;

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-2-methyl-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-2-methyl-3-phenylpropionyl-homoserine,

Applicants : M. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 23

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-4-pentenoyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-4-pentenoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-pentanoyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-pentanoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]5-pentyloxy-4-methylpentanoyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-4-methylpentanoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-methylbutanoyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-methylbutanoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylbutanoyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylbutanoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylthio-2-methyl-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylthio-2-methyl-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylsulfonyl-2-methyl-3-phenylpropionyl-homoserine lactone,

Applicants : A. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 24

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-

pentylsulfonyl-2-methyl-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-
pentyloxy-3-phenylpropionyl-methionine methyl ester,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-
methyl]pentyloxy-3-phenylpropionyl-methionine,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-
methyl]pentyloxy-3-phenylpropionyl-methionine sulfone methyl
ester,

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-
methyl]pentyloxy-3-phenylpropionyl-methionine sulfone
(Compound A),

2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-
pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl
ester,

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-
pentyloxy-3-naphth-2-yl-propionyl-methionine sulfone methyl
ester,

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-
pentyloxy-3-naphth-2-yl-propionyl-methionine sulfone,

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-
methyl]pentyloxy-3-naphth-1-yl-propionyl-methionine sulfone
methyl ester,

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-
methyl]pentyloxy-3-naphth-1-yl-propionyl-methionine sulfone,

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-
methyl]pentyloxy-3-methylbutanoyl-methionine methyl ester.

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-
methyl]pentyloxy-3-methylbutanoyl-methionine,

Applicants : M. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 25

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)methyl]pentyloxy-3-phenylpropionyl-homoserine lactone,

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-homoserine,

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)methyl]pentyloxy-3-methylbutanoyl-methionine methyl ester

1-(4-Biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Cyanobenzyl)-5-(4'-phenylbenzamido)ethyl-imidazole

1-(2'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Biphenylethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Bromo-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Trifluoromethoxy-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-(3',5'-dichloro)-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Methoxy-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-(3',5'-Bis-trifluoromethyl)-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)-4-methylimidazole

Applicants : W. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 26

1-(4-Biphenylmethyl)-5-(4-cyanophenoxy)-imidazole

5-(4-Cyanophenoxy)-1-(2'-methyl-4-biphenylmethyl)-imidazole

5-(4-Biphenyloxy)-1-(4-cyanobenzyl)-imidazole

5-(2'-Methyl-4-biphenoxy)-1-(4-cyanobenzyl)-imidazole

5-(4-(3',5'-dichloro)biphenylmethyl)-1-(4-cyanobenzyl)imidazole

1-(4-biphenylmethyl)-5-(1-(R,S)-acetoxy-1-(4-cyanophenyl)methyl)imidazole

1-(4-Biphenylmethyl)-5-(1-(R,S)-hydroxy-1-(4-cyanophenyl)methyl)imidazole

1-(4-Biphenylmethyl)-5-(1-(R,S)-amino-1-(4-cyanophenyl)methyl)imidazole

1-(4-biphenylmethyl)-5-(1-(R,S)-methoxy-1-(4-cyanophenyl)methyl)imidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(4-biphenyl)methyl)imidazole

1-(4-Cyanobenzyl)-5-(1-oxo-1-(4-biphenyl)methyl)imidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(3-fluoro-4-biphenyl)methyl)-imidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(3-biphenyl)methyl)-imidazole

5-(2-[1,1'-Biphenyl]vinylene)-1-(4-cyanobenzyl)imidazole

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)amino]-3-methoxy-4-phenylbenzene

1-(4-Biphenylmethyl)-5-(4-bromophenoxy)-imidazole

1-(3'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

Applicants : A. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 27

1-(3'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

1-(4'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

1-(3'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'3'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

1-(2'4'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

1-(2'5'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

1-(3'-Trifluoromethoxy-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

1-(2'-Fluoro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4-(2'-Trifluoromethylphenyl)-2-Chlorophenylmethyl)-5-(4-
cyanobenzyl) imidazole

1-{1-(4-(2'-trifluoromethylphenyl)phenyl)ethyl}-5-(4-
cyanobenzyl) imidazole

1-(2'-Trifluoromethyl-4-biphenylpropyl)-5-(4-cyanobenzyl)
imidazole

1-(2'-N-t-Butoxycarbonylamino-4-biphenylmethyl)-5-(4-
cyanobenzyl) imidazole

1-(2'-Aminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

1-(2'-Acetylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)
imidazole

Applicants : Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 28

1-(2'-Methylsulfonylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Ethylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Phenylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Glycinylinomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Methyl-4-biphenylmethyl)-2-chloro-5-(4-cyanobenzyl) imidazole

1-(2'-Methyl-4-biphenylmethyl)-4-chloro-5-(4-cyanobenzyl) imidazole

1-(3'-Chloro-2-methyl-4-biphenylmethyl)-4-(4-cyanobenzyl) imidazole

1-(3'-Chloro-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Trifluoromethyl-2-methyl-4-biphenylmethyl)-4-(4-cyanobenzyl) imidazole

1-(3'-Trifluoromethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Methoxy-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Chloro-4'-fluoro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Ethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-(2-Propyl)-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

Applicants : W. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 29

1-(2'-(2-Methyl-2-propyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Ethyl-4-biphenylmethyl)-5-(4-(1H-tetrazol-5-yl))benzyl)imidazole

1-[1-(4-Cyanobenzyl)imidazol-5-ylmethoxy]-4-(2'-methylphenyl)-2-(3-N-phthalimido-1-propyl)benzene

1-(3',5'-Ditrifluoromethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3',5'-Chloro-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3',5'-Dimethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-(N-Boc-aminomethyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)-imidazole

1-(3-Aminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Cyanobenzyl)-2-methyl-5-(2'-methylbiphenyl-4-yloxy)imidazole

5-(4-Cyanobenzyl)-1-(3-cyano-2'-trifluoromethylbiphenyl-4-ylmethyl)-imidazole

2-Amino-5-(biphenyl-4-ylmethyl)-1-(4-cyanobenzyl)imidazole

2-Amino-1-(biphenyl-4-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Butylbiphenyl-4-ylmethyl)-5-(4-cyanobenzyl)-imidazole

1-(3-Propylbiphenyl-4-ylmethyl)-5-(4-cyanobenzyl)-imidazole

1-(4-Biphenylmethyl)-4-(4-cyanobenzyl-2-methylimidazole

1-(4-Cyanobenzyl)-5-[(3-fluoro-4-biphenyl)methyl]imidazole

1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)-1-hydroxy]ethyl-2-methylimidazole

Applicants : N. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 30

1-(4-Cyanobenzyl)-5-(4-biphenylmethyl)-2-methylimidazole

1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)]ethyl-2-methyl imidazole

1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)]vinylidene-2-methylimidazole and

1-(4-Cyanobenzyl)-5-[2-(4-biphenyl)]vinylene-2-methylimidazole

1-(4-[Pyrid-2-yl]phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-[3-Methylpyrazin-2-yl]phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-(Pyrimidinyl-5-yl)phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Phenylpyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Phenyl-N-Oxopyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenylpyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-N-Oxopyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-(3-Trifluoromethoxyphenyl)-pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-(2-Trifluoromethylphenyl)-pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-2-Chloropyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-4-chloropyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Amino-3-phenylpyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

Applicants : N. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 31

1-(2-[Pyrid-2-yl]pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

N-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl)methyl]-5-(pyrid-2-yl)-2-amino-pyrimidine

N,N-bis(4-Imidazolemethyl)amino-3-[(3carboxyphenyl)oxy]benzene

N,N-bis(4-Imidazolemethyl)amino-4-[(3carboxyphenyl)oxy]benzene

N,N-bis(4-Imidazolemethyl)amino-3-[(3-carbomethoxyphenyl)-oxy]benzene

N,N-bis(4-Imidazolemethyl)amino-4-[(3-carbomethoxyphenyl)-oxy]benzene

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)aminomethyl-3-[(3-carboxyphenyl)oxy]benzene

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)aminomethyl-3-[(3-carbomethoxyphenyl)oxy]benzene

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)amino-3-(phenoxy)benzene

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)amino-4-(phenoxy)benzene

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)amino-4-(phenylthio)benzene

N-Butyl-N-[1-(4-cyanobenzyl)-5-imidazolemethyl]amino-4-(phenoxy)benzene

N-[1-(4-Cyanobenzyl)-5-imidazolemethyl]amino-4-(phenoxy)benzene

N-(4-Imidazolemethyl)amino-3-[(3-carboxyphenyl)oxy]benzene

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene

(±)-4-[(4-imidazolylmethyl)amino]pentyl-1-(phenoxy)benzene

Applicants : W. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 32

1-[(N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(n-butyl)amino)methyl]-4-(phenoxy)benzene

4-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(n-butyl)amino]-1-(phenylthio)benzene

(±)-4-[N-(1-(4-cyanobenzyl)-4-imidazolylmethyl)-N-(n-butyl)amino]-1-(phenylsulfinyl)benzene

3-[N-(4-imidazolylmethyl)-N-(n-butyl)amino]-N-(phenyl)benzenesulfonamide and

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)amino]-3-methoxy-4-phenylbenzene

4-{3-[4-(-2-Oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

4-{3-[4-3-Methyl-2-oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

4-{3-[4-(-2-Oxo-piperidin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

4-{3-[3-Methyl-4-(2-oxopiperidin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile

4-{3-[4-(2-Oxo-pyrrolidin-1-yl)-benzyl]-3H-imidazol-4-ylmethyl}-benzonitrile

4-{3-[4-(3-Methyl-2-oxo-2-H-pyrazin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile

4-{3-[2-Methoxy-4-(2-oxo-2-H-pyridin-1-yl)-benzyl]-3-H-imidazol-4-ylmethyl}-benzonitrile

4-{1-[4-(5-Chloro-2-oxo-2H-pyridin-1-yl)-benzyl]-1H-pyrrol-2-ylmethyl}-benzonitrile

4-[1-(2-Oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile

Applicants : S.W. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 33

4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile

4-[3-(2-Oxo-1-phenyl-1,2-dihydropyridin-4-ylmethyl)-3H-imidazol-4-ylmethyl]benzonitrile

4-[3-[1-(3-Chloro-phenyl)-2-oxo-1,2-dihydropyridin-4-ylmethyl]-3H-imidazol-4-ylmethyl]benzonitrile

or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.

79. (New) The method according to Claim 77 wherein an amount of a prenyl-protein transferase inhibitor and an amount of a microtubule-stabilizing agent comprising paclitaxel, docetaxel or epothilones are administered simultaneously.

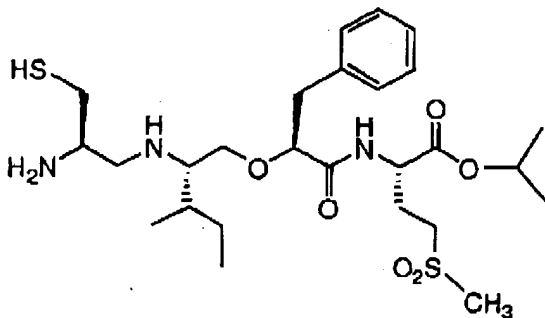
80. (New) The method according to Claim 77 wherein an amount of a microtubule-stabilizing agent comprising paclitaxel, docetaxel or epothilones and an amount of a prenyl-protein transferase inhibitor are administered consecutively.

81. (New) The method according to Claim 77 wherein the prenyl-protein transferase inhibitor is selected from:

2(S)-[2(S)-[2(R)-Amino-3-mercapto]-propylamino-

3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone

isopropyl ester (Compound A)



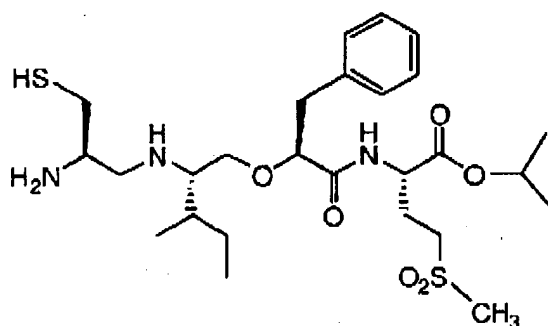
Applicants : A. Rosen et al.
U.S. Serial No. : 09/445,054
Filing Date : March 27, 2000
Page : 34

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile and

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.



82. (New) A pharmaceutical composition comprising an amount of a prenyl-protein transferase inhibitor and an amount of an antineoplastic agent which is a microtubule-stabilizing agent selected from paclitaxel, docetaxel or epothilone, the composition which achieves a synergistic effect for treating cancer in a mammal in need thereof.

83. (new) A method of preparing a pharmaceutical composition which comprises mixing an amount of a prenyl-protein transferase inhibitor and an amount of an antineoplastic agent which is a microtubule-stabilizing agent selected from paclitaxel, docetaxel or epothilone, said composition capable of achieving a synergistic effect for treating cancer in a mammal.